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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Appln. of: Yasuyuki KAWASHIMA

Appln. No.: 10/821,732

Filed: April 8, 2004

For: METHODS FOR MEASURING
BACTERIA, BACTERIA
MEASURING APPARATUSES,
AND STORAGE MEDIA FOR
STORING COMPUTER-
EXECUTABLE PROGRAMS FOR
ANALYZING BACTERIA

Examiner: Kailash C. Srivastava

Art Unit: 1657

Confirmation No.: 1524

Attorney Docket No: 11333-38(1-2002-090US)

AMENDED APPEAL BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This Appeal Brief is submitted pursuant to the Notice of Appeal filed December 16, 2010.

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REAL PARTY IN INTEREST

The real party in interest is Sysmex Corporation, the assignee of the above-referenced patent application.

RELATED APPEALS AND INTERFERENCES

This appeal involves the final rejection of all of the pending claims in U.S. Patent Application No. 10/821,732. There are no other related appeals or interferences involving this application or its subject matter.

STATUS OF CLAIMS

Claims 11, 14-21, and 25-26 are pending in the application and have been rejected. This appeal involves all of the pending claims, which are presently under a final rejection set forth in an Office Action mailed .

STATUS OF AMENDMENTS

The Examiner issued an Office Action on June 17, 2010 finally rejecting the appellants' pending claims. In reply to the Office Action of June 17, 2010, the appellant filed a response after final under 37 C.F.R. §116 and a Notice of Appeal on December 16, 2010. In the response, the appellant amended several of the pending claims to address matters of form. The Examiner issued an Advisory Action on February 10, 2011 and agreed to enter the appellants' amendment after final. Accordingly all of the amendments previously filed by the appellant have been acted upon by the Examiner during the course of prosecution.

SUMMARY OF CLAIMED SUBJECT MATTER

The invention relates to bacterial measuring apparatus used to automatically detect bacteria in a sample, where the apparatus includes the programmed capability for automatically detecting the presence of Bacillus or Coccus bacterium in the sample.

Claims 11 and 21 recite a sampling device and first and second detectors.

The apparatus employs detectors for determining particle size and fluorescence characteristics of a prepared sample. (pg. 10, ll. 9-35 and pg. 11, ll. 1-16). In one embodiment, the detector for determining particle size includes a pore for passing through bacteria and first and second electrodes. The particle size is determined from the change in electrical resistance of a sample over time when the prepared sample passes through the pore. In another embodiment, a detector determines particle size information by scattered light pulse width or scattered light intensity emitted by particles using flow cytometry. In these methods, particle size information includes information reflecting particle diameter, particle width in a direction perpendicular to the particle diameter, particle volume, or the like.

A detector is also provided for detecting the intensity of fluorescent light emitted by fluorescently stained particles via flow cytometry. (pg. 11, ll. 1-16). A fluorescent dye for bonding to components of the bacteria and emitting fluorescent light is used in the bacteria fluorescent stain. For example, bacteria in a specimen may be uniquely stained using a nucleic acid staining dye which uniquely bonds with intracellular DNA and RNA of the bacteria. By way of example, polymethene dyes may be used. (¶pg. 7, ll. 1-10). A laser light irradiates a flowing sample fluid which contains target particles such as bacteria and cells. Optical information concerning scattered light and fluorescent light generated when the particles pass through the laser irradiation area is detected. The forward scattered light signal reflects the size of the particle, and the fluorescent light signal reflects the degree of staining of the particle which was fluorescently stained beforehand.

The apparatus includes a sample preparation unit provided with a specimen holding unit (201), reagent holding unit (202), incubator (204) or reaction unit, and a movable dispenser (205). An embodiment of the apparatus is illustrated by FIG. 2 of the appellant's drawing below.

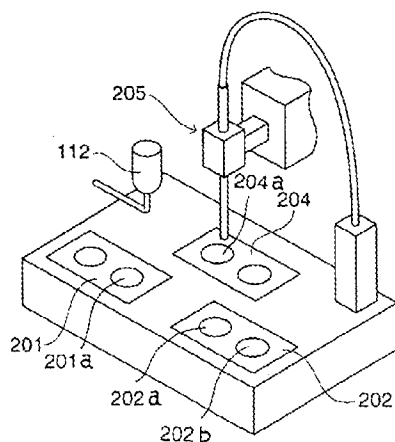


Fig. 2

A receptacle (201a) holds a specimen, a receptacle (202a) holds a dilution fluid, and a receptacle (202b) holds a staining fluid. A receptacle (204a) is provided for mixing the specimen and the reagents. The dispenser respectively suctions predetermined amounts of specimen and dilution fluid or staining fluid and discharges the specimen and the fluids into the receptacle (204a) where the fluids are mixed. The prepared sample is then suctioned by the dispenser and supplied to a sample receptacle (112).

As illustrated by FIG. 3 of the appellant's drawing below, the sample receptacle (112) is connected to detection unit that includes a flow cell (107). (pg. 14, ll. 20-33, pg. 15, line 1).

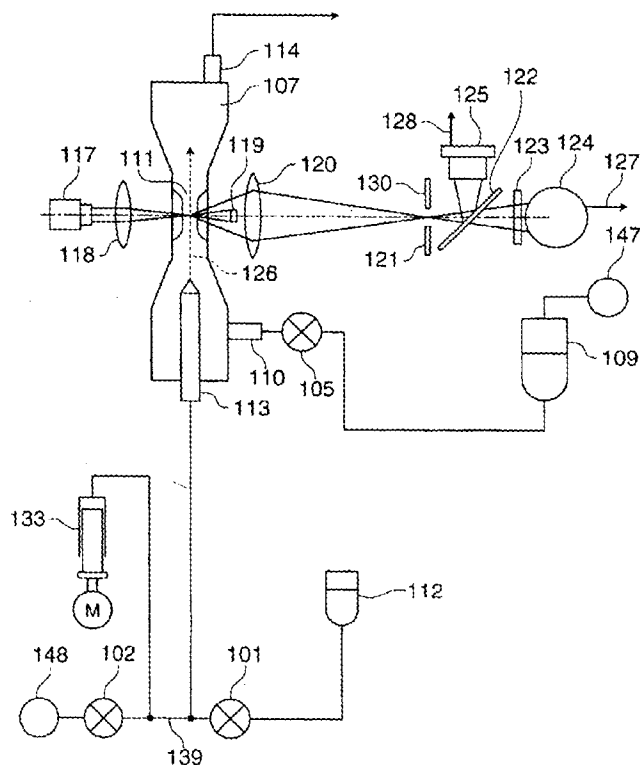


Fig. 3

The flow cell (107) is provided with a nozzle (113) that discharges sample fluid toward an orifice (111). A laser light source (117) irradiates the fluid sample with a laser beam and various types of optical components (118, 119, 120, 130, 121, 122, and 123) condense the fluorescent light and forward scattered light emitted from the particles in the sample fluid. A photomultiplier tube (124) detects the condensed fluorescent light and generates a fluorescent light signal (127), and a photodiode (125) detects the forward scattered light and generates a scattered light signal (128).

Claims 11 and 21 recite a processor and a memory including programs

The apparatus further includes an analysis control unit that includes an information processor (134) that is provided with an analyzer (141), memory (145), and controller (146). (pg. 15, ll. 25-33, pg. 16, ll. 1-11, FIG.4). The analyzer is, in turn, provided with a scattergram generator (142), analysis unit (143), and a

determining unit (144). The memory stores analysis programs for analyzing the signals obtained from particles in the sample fluid, and control programs for controlling the operation of each part of the apparatus.

The analyzer (141) in the information processor (134) analyzes the fluorescent light the signal from (127) and forward scattered light signal (128) according to a program stored in the memory (145). (pg.19, ll. 14-25). These signals are received by the scattergram generator (142). The scattergram generator calculates the forward scattered light intensity Fsc from the maximum peak value of the forward scattered light signal (128) and record this as particle size information. Similarly, the fluorescent light intensity FL is calculated from the fluorescent light signal (127) and is recorded as fluorescent light information. Then, scattergram generator creates a two-dimensional scattergram plotting fluorescent intensity (FL) FL on the X axis, and forward scattered light intensity (Fsc) on the Y axis. (pg. 19, ll. 30-33, pg. 20, ll. 1-4). Comparative scattergrams are illustrated by FIGs. 7 and 8 of the appellant's drawing below.

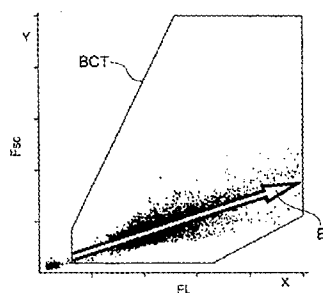


Fig. 7

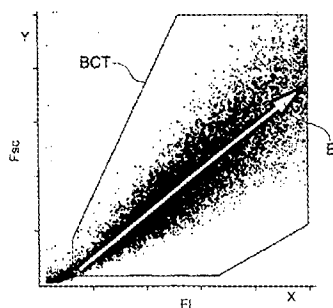


Fig. 8

The scattergrams are composed of dots corresponding to individual particles on a coordinate space having particle size on the vertical axis, and fluorescent light information on the horizontal axis. When the particle properties differ, differences occur in the distribution of dots on the scattergram. Surprisingly, when Bacillus - containing samples and Coccus-containing samples are compared, the size information of both are substantially identical, but the obtained fluorescent light information tends to be greater for the Bacillus than for the Coccus.

In the scattergram shown above, FIG. 7 is an exemplary scattergram obtained from a specimen containing Bacillus, and FIG. 8 an exemplary scattergram obtained from a specimen containing Coccus. (pg. 12, ll. 2-31). As can be seen by the differences in the plots above, the presence of Bacillus or Coccus bacteria in the sample results in differences in the dot distribution on the scattergram. In accordance with an aspect of the invention, a determination as to whether the bacteria in a sample is Bacillus or Coccus is based on the differences in this distribution. (pg. 11. Ll. 1-33, pg. 12, line 1). The differences in the distribution of dots in a Bacillus specimen and Coccus specimen are expressed in the slopes of the distributions.

The region labeled "BCT" is the region in which dots corresponding to bacteria appear. The population of dots corresponding to bacteria in the scattergrams is distributed so as to extend in a fixed direction (from lower left to upper right). In the coordinate space of the scattergrams, the slope having this "fixed direction" is the slope of the distribution. When FIGS. 7 and 8 are compared, the slope of the distribution is larger in the Coccus-containing specimen (FIG. 8) than in the Bacillus -

containing specimen (FIG. 7). From this fact, in accordance with the present invention, a determination as to whether bacteria in a specimen is Bacillus or Coccus is based on the slope of the distribution. The slope of the distribution is determined in the direction of maximum variance of the dots representing the bacteria, and the slope of the distribution may be determined by determining the slope in the maximum variance direction. A slope of approximate expression calculated from the dots representing the bacteria may also be used as the slope of the distribution. (pg.12, ll. 2-31).

The analysis unit (143) determines the variance of the dots of particles within the BCT region in the X-Y two-dimensional space, and determines the directional vector E in which there is maximum variance through the center of the variance. The determined directional vector E is converted to a unit vector (a vector having a length of 1). (pg. 20, ll. 5-15, FIG. 9). The unit vector is broken down into a component in the X axis direction and a component in the Y axis direction, and the magnitude of the component in the Y axis direction is designated as "P," which is a value representing the degree of slope of the directional vector relative to the X axis.

The determining unit (144) compares the value of P to a predetermined value "A" (for example, $A=0.68$). (pg. 20, ll. 29-33, pg. 12, ll. 1-21). When $P>A$, the bacteria included in the specimen is determined to be Coccus, whereas when $P<A$, the bacteria is determined to be Bacillus. An example of the screen output to the liquid crystal touch panel (11) (FIG. 1) is illustrated by FIG. 10 of the appellant's drawing below.

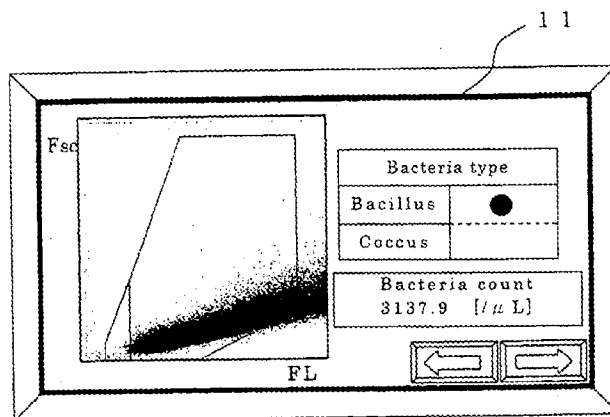


Fig. 10

The scattergram, the bacteria determination result, and the bacteria count are displayed. In the spaces indicating the determination result for the type of bacteria, a mark is displayed in the [Bacillus] category to indicate that the determination result is Bacillus.

The relative magnitude of P and A, and the degree to which P differs from A is used to evaluate the reliability of the determination result. When P is less than A, the determination unit (144) compares the parameter P and a predetermined value “B,” which is less than A (for example, B=0.60). Further, when $P < B$, the particles contained in the specimens are determined to be Bacillus, and when $A > P$ and $P \geq B$, the determination is deemed difficult. (pg. 25, ll. 11-20). Screens corresponding to these determination results are output to the liquid crystal touch panel 11. Furthermore, the scattergram, and the bacteria count are combined and output to the liquid crystal touch panel. An example of the screen output on the liquid crystal touch panel (11, FIG. 1) is illustrated by FIG. 19 of the appellant’s drawing below.

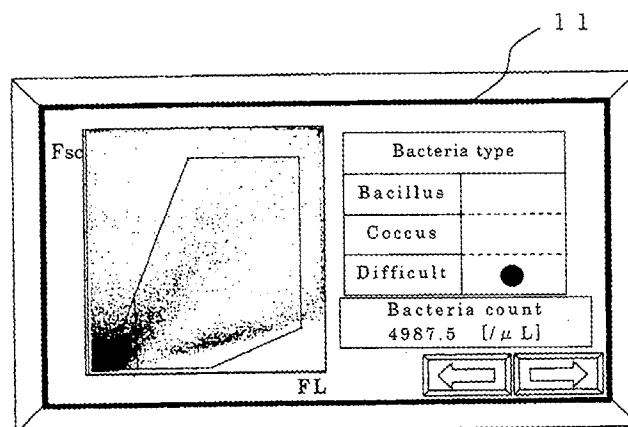


Fig. 19

The two-dimensional scattergram, bacteria typing determination result, and bacteria count are displayed. In the spaces indicating the determination result for the type of bacteria, a mark is displayed in the [Determination Difficult] category as a warning to indicate that the bacteria typing determination result for this specimen is difficult.

Furthermore, when outputting the bacteria typing determination result, the degree of reliability of the determination result may also be output. (pg. 26, ll. 14-32). For example, when bacteria in a specimen is determined to be either Bacillus or Coccus, the degree of dissociation of the calculated P value and the predetermined value A may be calculated and output. Generally, the larger the degree of dissociation, the greater the reliability of the determination result. When Coccus is determined ($P > A$), the degree of dissociation between the P value and the predetermined value A is calculated: the larger the degree of dissociation, the higher the reliability of a result determining that the bacteria is Coccus. Correspondingly, when Bacillus is determined ($P < B$), the degree of dissociation between the P value and the predetermined value B is calculated. The greater the degree of dissociation, the higher the reliability of the result determining the bacteria is Bacillus .

GROUND OF REJECTION TO BE REVIEWED ON APPEAL

The Examiner rejected claims 11, 14-17 and 25 under 35 U.S.C. § 102(b) as anticipated by Wallner et al. The first issue to be decided on appeal is whether claims 11, 14-17 and 25 are unpatentable under 35 U.S.C. § 102(b) in view of Wallner et al.

The Examiner also rejected claims 11, 14-15, 17, 19 and 25 under 35 U.S.C. § 102(b) as being unpatentable over Fukuda et al. The second issue to be decided on appeal is whether claims 11, 14-15, 17, 19 and 25 are unpatentable under 35 U.S.C. § 102(b) over Fukuda et al.

The Examiner also rejected claims 11, 14-21, and 25-26 under 35 U.S.C. § 103(a) as being unpatentable over Wallner et al. and Fukuda et al. in view of Dow et al. The third issue to be decided on appeal is whether claims 11, 14-21, and 25-26 are unpatentable under 35 U.S.C. § 103(a) in view of Wallner et al. and Fukuda et al. and Dow et al.

The claims at issue are set forth in the Claims Appendix.

ARGUMENT

I. CLAIM REJECTION UNDER 35 U.S.C. § 102(b)

The appellant first asserts that the pending claims do not lack novelty in view of Wallner et al. or Fukuda et al. It is well settled that anticipation requires the presence in a single prior art disclosure all of the elements of the claimed invention arranged as in the claim. *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548, 220 USPQ 193, 198 (Fed. Cir. 1983). With respect to this requirement, the phrase “arranged as in the claim” has been interpreted to mean that all of the claimed limitations must be arranged or combined in the same way as recited in the claims. *Net MoneyIN Inc. v. VeriSign Inc.*, 545 F. 3d 1359, 1370, 88 USPQ2d 1751, 1758-59 (Fed. Cir. 2008). The appellant asserts that neither of the cited references anticipate the appellants’ claims in view of the failure of these references to disclose all of the elements of the claimed bacteria measuring apparatus.

A. Rejection of Independent Claims Under 35 U.S.C. §102(b) in view of Wallner et al.

Independent Claims 11 and 25

Each of independent claims 11 and 25 call for a sampling device for processing a sample comprising fluorescently stained bacteria. These claims also recite a memory including programs that enable the processor to execute operations comprising creating a scattergram of the bacteria using the size information and the fluorescence information as parameters, and obtaining a maximum variance direction of distribution of the bacteria, as in claim 11, or obtaining a maximum variance direction of distribution of the bacteria in a scattergram which is created by using the size information and the fluorescence information obtained from the bacteria, as in claim 25. These claims further recite a memory including programs that enable determining whether the bacteria in the sample are bacillus or coccus based on the maximum variance direction of the distribution. The appellant asserts that claims 11 and 25 are not anticipated by Wallner et al. at least because Wallner et al. fail to disclose these elements.

The appellant asserts that Wallner et al. fail to suggest or disclose a bacteria measuring apparatus that includes a processor and a memory including programs configured to create a scattergram of the bacteria using size information and fluorescence information as parameters and obtain a maximum variance direction of a distribution of the bacteria in the scatter gram. Wallner et al. fail to suggest or disclose the appellants' claimed processor that analyzes the distribution and determines whether the bacteria in the sample are Bacillus or Coccus based on the maximum variance of the distribution. Instead, Wallner et al. disclose a technique for sorting selected cell types from water, sediment, and activated sludge. (Pg. 4223, left colume, first full paragraph). Although Wallner et al. produce scattergrams from flow cytometry analysis as shown in FIG. 4, there is no disclosure of obtaining a maximum variance direction and determining whether the bacteria in the sample are Bacillus or

Coccus based on the maximum variance direction of the distribution, as recited by independent claims 11 and 25. Instead, Wallner et al. use a gating technique to sort the different kinds of organisms. (See, paragraphs referencing FIGs. 2 and 4).

In addition to the cited reference, the Examiner relies upon subject matter disclosed in an Internet website. (Advisory Action, pg. 2, section 2). An excerpt from the currently-available referenced Internet document appears in the evidence appendix. The appellant asserts that this information is not part of the published reference to Wallner et al. Accordingly, to the extent that the instant rejection relies on information from another source, the rejection cannot be based on novelty under Section 102(b). Although the Examiner asserts that a supporting document is permissible to formulate a rejection under Section 102, the Examiner fails to point to any legal authority for this conclusion. (Advisory Action, pg. 2, section 2). To the contrary, the Federal Circuit has unambiguously stated that a demonstration of anticipation requires that the four corners of a single, prior art document describe every element of the claimed invention. *Xerox Corp. v. 3Com Corp.*, 458 F.3d 1310, 1322, 80 USPQ 1916, 1927 (Fed. Cir. 2006). The forgoing notwithstanding, the appellant asserts that, regardless of the status of the additionally-cited Internet information, as stated above, Wallner et al. do not disclose the apparatus recited by claims 11, 14-17 and 25. Accordingly, this rejection should be overturned.

The Examiner's rejection appears to be based, at least in part, upon the notion that claim elements recite functional intended use limitations and do not carry patentable weight. (Advisory Action, pg. 2, section 2). The applicants assert that claims 11 and 25 recite a sampling device, first and second detectors, a processor, and a memory including programs. The programs are recited in the context of their operational attributes. The appellant asserts that even if the operation of the programs can be construed as functional, the recited operational aspects are associated with the memory and define a particular capability that is served by the programs in the memory. The appellant asserts that the operational attributes of the programs stored in the memory of the recited apparatus must be evaluated and considered for what it conveys to a person skilled in the art.

The appellant further asserts that these claims recite aspects of the memory that enable the processor to execute operations. Contrary to the assertion that a functional intended use of the device is recited, the appellant asserts these claims recite an apparatus that includes a structural configuration that performs the recited analysis. To the extent that the appellant's claims could be construed to include functional language, the appellant asserts that a functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used. Claims that include a functional limitation in association with an element to define a particular capability or purpose that is served by the recited element properly define the scope of a patent claim. *See Innova/Pure Water Inc. v. Safari Water Filtration Sys. Inc.*, 381 F.3d 1111, 1117-20, 72 USPQ2d 1001, 1006-08 (Fed. Cir. 2004). Here, claim 11 recites a memory including programs configured to analyze bacteria from information generated by the claimed apparatus. Accordingly, the appellant asserts that claim 11 recites a particular configuration for performing the recited bacteria analysis.

Dependent Claim 14

Dependent claim 14 builds on the features recited by claim 11 and specifically recites a computational analysis involving obtaining a slope of the maximum variance that is executed by the processor. This feature is not disclosed by Wallner et al. As described above, Wallner et al. sorts microorganisms and does not characterize the scattergrams based on a slope of maximum variance.

Dependent Claims 15-17

Claims 15 describes the detection of scatter light by the first detector and claim 16 recites the structural characteristics of the first detector. The output of this detector is analyzed as size information from each of the bacterial in the sample. This claim is allowable at least in view of its dependence from claim 11.

Claim 16 describes structural features of the first detector. The appellant cannot identify disclosure of the recited features by Wallner et al. Further, this claim is allowable at least in view of its dependence from claim 11.

Claim 17 describes further structural features of the bacteria measuring apparatus. This claim is allowable at least in view of its dependence from claim 11.

Thus, Wallner et al. fail to disclose all of the elements of the claimed invention arranged as in claims 11, 14-17 and 25. Accordingly, this rejection should be overturned.

B. Rejection of Claims Under 35 U.S.C. §102(b) in view of Fukuda et al.

Independent Claims 11 and 25

Each of independent claims 11 and 25 call for a sampling device for processing a sample comprising fluorescently stained bacteria. These claims also recite a memory including programs that enable the processor to execute operations comprising creating a scattergram of the bacteria using the size information and the fluorescence information as parameters, and obtaining a maximum variance direction of distribution of the bacteria, as in claim 11, or obtaining a maximum variance direction of distribution of the bacteria in a scattergram which is created by using the size information and the fluorescence information obtained from the bacteria, as in claim 25. These claims further recite a memory including programs that enable determining whether the bacteria in the sample are bacillus or coccus based on the maximum variance direction of the distribution. The appellant asserts that claims 11 and 25 are not anticipated by Fukuda et al. at least because Fukuda et al. fail to disclose these elements.

Fukuda et al. disclose a flow cytometer measuring particle size of microorganisms in a culture, the assaying program determines first and second particle-size distributions from scattered light and determines the differences in the first and second particle-size distributions. The appellant asserts that Fukuda et al.

merely disclose a device that can distinguish among several different types of bacteria, but does not include components configured to perform the analysis recited by claims 11 and 25. In particular, there is no disclosure of a memory including programs that enable a processor to obtain a maximum variance direction of distribution of the bacteria in the scattergram or to determine whether the bacteria in the sample are Bacillus or Coccus based on the maximum variance direction of the distribution. Further, as more fully described below, Fukuda et al. contains no teaching or suggestion of utilizing fluorescence information as a parameter for creating a scattergram, as recited by independent claims 11 and 25. Accordingly, Fukuda et al. do not anticipate claims 11 and 25.

Dependent Claim 14

Dependent claim 14 builds on the features recited by claim 11 and specifically recites a computational analysis involving obtaining a slope of the maximum variance that is executed by the processor. This feature is not disclosed by Fukuda et al. Instead, like Wallner et al., Fukuda et al. merely sort microorganisms based on the general appearance of the bacteria in the scatterplots and do not characterize the scattergrams based on a slope of maximum variance. For example, with respect to bacilli, Fukuda et al. investigate the differences in the scatterplots resulting from differences in the culture used with urine samples. (Col. 13, ll. 64-67, Col. 14, ll. 1-60).

Dependent Claims 15, 17, and 19

Claims 15, 17 and 19 describe further structural features of the bacteria measuring apparatus. This claim is allowable at least in view of their dependence from claim 11.

Thus, Fukuda et al. fail to disclose all of the elements of the claimed invention arranged as in claims 11, 14-15, 17, 19 and 25. Accordingly, this rejection should be overturned.

II. CLAIM REJECTION UNDER 35 U.S.C. § 103(a)

Upon consideration of the scope and content of the prior art, the differences between the claimed invention and the prior art, and the level of ordinary skill in the art in relation to combining the cited references, it is apparent that Wallner et al. in view of Fukuda et al. and further in view of Dow et al. do not establish that the appellant's claims are obvious in view of these references.

In determining whether the claimed subject matter would have been *prima facie* obvious to one skilled in the art at the time the invention was made, the trier of fact must consider (1) the scope and content of the prior art, (2) the differences between the art and the claims at issue, and (3) the level of ordinary skill in the art. Other objective evidence may be considered, such as commercial success, a long-felt need, failure of others, copying, praise by persons in the industry, departure from accepted principles, and wide-spread recognition in the art of the invention's significance. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966).

A. The Scope And Content of the Cited Prior Art

Wallner et al.

Wallner et al. disclose a technique for sorting selected cell types from water, sediment, and activated sludge. (Pg. 4223, Abstract). Wallner et al. note that problems occur in observing RNA gene fragments in cultivation-independent analysis methods of microbial organisms. (Pg. 4223, left-hand column). Wallner et al. propose to overcome this problem through the use of flow cytometry (FCM) with staining by fluorescent antibodies. (Pg. 4223, right-hand column). Wallner et al. describe a gating technique to sort the different kinds of organisms. (See, paragraphs referencing FIGs. 2 and 4). Wallner et al. produce scattergrams from the flow cytometry analysis plotted as probe fluorescence versus forward scatter. (FIGs. 4 and

7.) Wallner et al. note limitations of the described technique including low sensitivity and high signal noise. (Pg. 4249, left-hand column, Pg. 4250, left-hand column).

Fukuda et al.

Fukuda et al. disclose a method and device for distinguishing between Bacilli, Staphylococci, Streptobacilli, Streptococci, and yeast fungi based on optical information obtained from scattered light. (Abstract; col. 3, ll. 10-18, 21-27, and 42-50; Col. 3, line 67 to Col. 4, line 7; Col. 6, ll. 55-61; Col. 7, ll. 7-16; Col. 13, ll. 11-24). Fukuda et al. discloses the use of the dual parameters of intensity and duration of emitted scattered light. (Col. 2, ll. 11-20). Thus, the particle-size distribution graphs described by Fukuda et al. have horizontal and vertical axes that correspond, respectively, to duration (Fscw) and intensity (Fsc) of emitted scattered light. (Col. 7, ll. 10-12; Col. 8, ll. 4-6; FIGS. 9-20, and 29).

Dow et al.

Dow et al. disclose analysis of particle size distribution in urine samples using a Coulter Counter (ZBI). The samples were analyzed to evaluate the particle and cell volume distributions of microbial populations. (Pg. 387, left-hand column, FIGs. 1 and 3). Samples were analyzed by at different detector amplifications and the data was recorded on XY plots. (Pg. 388 right-hand column, FIG. 3). The results are compared with standard bacterial analysis using cultures and incubation and microscopic examination. (Pg. 389, Table 1). A plot of relative number versus cell volume is characterized for different types of bacteria. (Pg. 389, left-hand column, Table 2 and FIG. 4).

B. The Differences Between The Claims and The Cited References

Independent Claims 11 and 25

The appellant asserts that Wallner et al. fail to suggest or disclose a bacteria measuring apparatus that includes a processor and a memory including programs configured to create a scattergram of the bacteria using size information and fluorescence information as parameters and obtain a maximum variance direction of a distribution of the bacteria in the scatter gram. Wallner et al. fail to suggest or disclose the appellants' claimed processor that analyzes the distribution and determines whether the bacteria in the sample are Bacillus or Coccus based on the maximum variance of the distribution. Instead, Wallner et al. disclose a technique for sorting selected cell types from water, sediment, and activated sludge. (Pg. 4223, left column, first full paragraph). Although Wallner et al. produce scattergrams from flow cytometry analysis as shown in FIG. 4, there is no disclosure of obtaining a maximum variance direction and determining whether the bacteria in the sample are Bacillus or Coccus based on the maximum variance direction of the distribution, as recited by independent claims 11 and 25. Instead, Wallner et al. use a gating technique to sort the different kinds of organisms. (See, paragraphs referencing FIGS. 2 and 4).

Fukuda et al. contains no teaching or suggestion of utilizing fluorescence information as a parameter for creating a scattergram, as recited by independent claims 11 and 25. Similarly, Fukuda et al. contains no teaching or suggestion of analyzing fluorescence information to obtain a bacteria analysis result, as recited by independent claim 25. On the contrary, Fukuda et al. teaches a different method from "fluorescently stained bacteria"—such as those recited in each of independent claims 11 and 25—and invokes instead the dual parameters of intensity and duration of emitted scattered light. (Col. 2, ll. 11-20). Thus, the particle-size distribution graphs described in Fukuda et al. have horizontal and vertical axes that correspond, respectively, to duration (Fscw) and intensity (Fsc) of emitted scattered light. (Col. 7, lines 10-12; col. 8, lines 4-6; FIGS. 9-20, FIG. 29). This contrasts with scattergrams having horizontal and vertical axes that correspond, respectively to fluorescent light intensity (FL) and forward scattered light intensity (Fsc), such as those shown, for example, in FIGS. 7-8 and 11-17 of Applicant's

specification and reflected as size information and fluorescence information in the appellant's claims.

The appellant further asserts that Fukuda et al. fail to suggest or disclose a bacteria measuring apparatus including a sampling device, and first and second detectors, as described above. While Fukuda et al. disclose a flow cytometer measuring particle size of microorganisms in a culture, the assaying program determines first and second particle-size distributions from scattered light and determines the differences in the first and second particle-size distributions. The appellant asserts that Fukuda et al. merely disclose a device that can distinguish among several different types of bacteria, but does not include components configured to perform the analysis recited by claims 11 and 25. In particular, there is no disclosure of a memory including programs that enable a processor to obtain a maximum variance direction of distribution of the bacteria in the scattergram or to determine whether the bacteria in the sample are Bacillus or Coccus based on the maximum variance direction of the distribution.

Dow et al. do not suggest or disclose a bacteria measuring apparatus having a processor and memory including programs that obtain a maximum variance direction of distribution of the bacteria in a scattergram to determine if the bacterial are Bacillus or Coccus, as recited by claims 11 and 25.

Dependent Claim 14

As asserted above, dependent claim 14 builds on the features recited by claim 11 and specifically recites a computational analysis involving obtaining a slope of the maximum variance that is executed by the processor. This feature is not disclosed by Fukuda et al. Instead, like Wallner et al., Fukuda et al. merely sort microorganisms based on the general appearance of the bacteria in the scatterplots and do not characterize the scattergrams based on a slope of maximum variance. For example, with respect to bacilli, Fukuda et al. investigate the differences in the scatterplots resulting from differences in the culture used with urine samples. (Col. 13, ll. 64-67,

Col. 14, ll. 1-60). Dow et al. do not overcome the deficiencies of Wallner et al., Fukuda et al.

Dependent Claims 15-16, 17, 19, and 26

Claims 15-16, 17 and 19 describe further structural features of the bacteria measuring apparatus. These claims are allowable at least in view of their dependence from claim 11.

Claim 26 is allowable at least in view of the forgoing remarks pertaining to claim 25, from which it depends.

Dependent Claims 18

Dependent claim 18 recites further aspects of the appellant's bacteria measuring apparatus and includes specimen handling and fluorescent die mixing components. As asserted above, Fukuda et al. and Dow et al. do not disclose any type of fluorescent stain. Further, Fukuda et al. explicitly state that a staining method is not suited to assaying large quantities of specimens. (Col. 2, ll. 15-20). Although Wallner et al. describe a hybridization and DNA staining technique, there is no suggestion of the sample handling equipment and component configuration recited by claim 18. (Pg.4224, right-hand column).

Dependent Claims 20

Dependent claim 20 depends from dependent claim 19 and recites a feature of the display in which a warning is exhibited with there is a difficulty in indentifying whether the bacteria in the sample is Bacillus or Coccus. The appellant asserts that none of the cited references suggest or disclose this feature. The appellant asserts that the use of the term "difficult" is defined in the specification of the instant application and is based on numerical analysis of the scatterplot. (See for example, ¶¶0095-0096). The cited references fail to suggest or disclose any type of numerical analysis that would result in a determination of difficulty as expressed in claim 20. Since none of the cited references suggest or disclose the determining the maximum variance

distribution as recited in claims 11 and 19, there can be no suggestion of the numerical analysis required to ascertain when determination of Bacillus or Coccus in a measurement sample is difficult.

Dependent Claim 21

Dependent claim 21 depends from claim 19 and recites a feature of the display in which a degree of reliability for the type of bacteria is exhibited. The appellant asserts that the cited references fail to suggest or disclose reliability assessment that is exhibited on a display as claimed. Although Wallner et al. describe shortcomings of their flow cytometry technique, they do not suggest any method of assessing reliability based on the maximum variance distribution in a scattergram. (Pg. 4249, left-hand column, Pg. 4250, left-hand column).

C. The Combined Cited References Fail To Disclose The Claimed Invention

A person skilled in this art is at least a highly trained engineer have the necessary education and experience to deal with highly complex, computer-driven mechanical and analysis systems. The appellant asserts that upon reviewing the cited references, a person skilled in the art would not understand the disclosure of the bacterial measurement apparatus recited by the appellant's pending claims. As asserted above, the cited references disclose different types of analysis devices that use different methods from the claimed apparatus. The particle size sorting with the disclosed FCM device employing a gating technique of Wallner et al. substantially differs from the Coulter Counter and particle size sorting of Dow et al. Further, Fukuda et al. point to the difficulty of using staining techniques for fluoroscopy. Moreover, there is no description within these references of how one skilled in the art might combine the equipment and methods to arrive at the appellants claimed invention.

The appellant further asserts that even if one skilled in the art were somehow motivated to combine Wallner et al., Fukuda et al., and Dow et al., the combination would not provide all of the appellants claim elements. Wallner et al. do not disclose At a minimum, Fukuda et al. do not teach or suggest (a) “a control unit configured for performing operations comprising: creating a scattergram of the bacteria using...fluorescence information as parameters; analyzing distribution of the bacteria in the scattergram; and determining whether the bacteria in the sample are bacillus or Coccus based on an analysis result,” as required by independent claim 11; or (b) “a control unit configured for performing operations comprising: analyzing...fluorescence information obtained from the bacteria; and determining whether the bacteria in the sample are Bacillus or Coccus based on an analysis result,” as required by the appellant’s claims.

The appellant asserts that the particle size distribution and analysis of Dow et al., even in combination with Wallner et al. and Fukuda et al. does not suggest or disclose the appellant’s size and fluorescence detectors and processor that determine whether the bacteria in the sample are Bacillus or Coccus based on the maximum variance direction of the distribution. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. See *In re Royka*, 490 F.2d 981, 985, 180 USPQ 580, 583 (CCPA 1974). Further, all words in a claim must be considered in judging the patentability of that claim against the prior art. *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

None of the cited references suggest or disclose obtaining a maximum variance direction of distribution of the bacteria in a scattergram which is created by using the size information and the fluorescence information obtained from the bacteria. These references further fail to suggest or disclose a memory including programs that enable determining whether the bacteria in the sample are bacillus or coccus based on the maximum variance direction of the distribution.

The appellant asserts that, the above arguments regarding the dependent claims notwithstanding, the dependent claims are not obvious at least in view of the

failure to establish the obviousness of the independent claims. If an independent claim is nonobvious under Section 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 1076, 5 USPQ2d 1596,1600 (Fed. Cir. 1988). Accordingly, the appellant requests that the obviousness rejection be overturned.

III. CONCLUSION

For the reasons set forth above, it is submitted that claims are not obvious over in view of anticipated by nor obvious in view of Wallner et al., Fukuda et al., and Dow et al. Accordingly, this rejection is improper and the appellant respectfully requests that it be reversed.

Respectfully submitted,

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CLAIMS APPENDIX

The claims under appeal are listed below.

11. A bacteria measuring apparatus comprising:
 - a sampling device for processing a sample comprising fluorescently stained bacteria;
 - a first detector for detecting size information from each of the bacteria in the sample;
 - a second detector for detecting fluorescence information expressing an intensity of fluorescent light emitted from each of the bacteria in the sample;
 - a processor;
 - a memory including programs that enable the processor to execute operations comprising:
 - creating a scattergram of the bacteria using the size information and the fluorescence information as parameters;
 - obtaining a maximum variance direction of distribution of the bacteria in the scattergram by analyzing the distribution in the scattergram; and
 - determining whether the bacteria in the sample are bacillus or coccus based on the maximum variance direction of the distribution.
14. The apparatus of Claim 11, wherein the analyzing is performed so as to obtain a slope of the maximum variance direction.
15. The apparatus of Claim 11, wherein the first detector detects scattered light obtained from the bacteria.
16. The apparatus of Claim 11, wherein the first detector comprises:
 - a member having a pore for passing the bacteria; and
 - first and second electrodes,

wherein the first detector detects electrical resistance between the first and the second electrodes, which is generated by passage of the bacteria through the pore.

17. The apparatus of Claim 11, further comprising:
 - a flow cell for flowing the sample comprising the bacteria; and
 - a laser light source for irradiating the sample within the flow cell;
 - wherein the first detector detects scattered light emitted from the bacteria in the sample; and
 - wherein the second detector detects the fluorescent light emitted from the bacteria in the sample.
18. The apparatus of Claim 11, further comprising:
 - a specimen holding part for placement of a specimen;
 - a reagent holding part for placement of fluorescent dye reagent; and
 - a mixing part for preparing the sample by mixing the specimen and the fluorescent dye reagent.
19. The apparatus of Claim 11, further comprising a display for displaying a result determined by the processor.
20. The apparatus of Claim 19, wherein the display exhibits a warning when it is difficult to determine a type of the bacteria.
21. The apparatus of Claim 19, wherein the display exhibits a degree of reliability for a type of the bacteria determined by the processor.
25. A bacteria measuring apparatus comprising:
 - a sampling device for processing a sample comprising fluorescently stained bacteria;

a first detector for detecting size information from each of the bacteria in the sample;

a second detector for detecting fluorescence information expressing an intensity of fluorescent light emitted from each of the bacteria in the sample;

a processor;

a memory including programs that enable the processor to execute operations comprising:

obtaining a maximum variance direction of distribution of the bacteria in a scattergram which is created by using the size information and the fluorescence information obtained from the bacteria; and

determining whether the bacteria in the sample are bacillus or coccus based on the maximum variance direction of the distribution.

26. The apparatus of claim 25, further comprising a display,

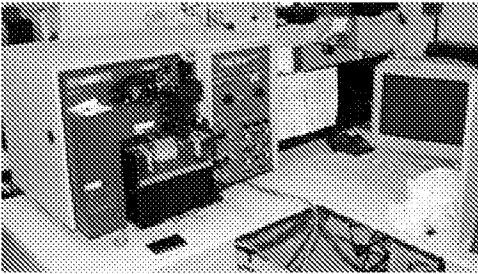
wherein the operations further comprise creating the scattergram based on the size information and the fluorescence information obtained from the bacteria, and wherein the display exhibits the scattergram.

EVIDENCE APPENDIX

The appellant has not submitted evidence pursuant to 37 CFR §§ 1.130, 1.131 or 1.132, or other evidence in the instant application.

The appellant submitted the following evidence during prosecution of the application under appeal. The following reference was cited by the Examiner in the Office Action of June 17, 2010, at page 3: <http://www.biomedika.com>. The following is the appellant's retrieval of the information at the referenced website and appears in the appellant's response of December 16, 2010, at page 6.

BD FACStar Plus Cell Sorter Flow Cytometer



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Description: One BD FACStar Plus Cell Sorter Flow Cytometer with Dual Lasers, Mac G4 and Cell Quest Pro Upgrade for Mac OS X. Includes: one Spectra Physics Model 127 NeHe air cooled laser; one Coherent Innova 70 water cooled laser; Miscellaneous. Complete unit in fairl good condition. Respond to receive price with ordering information.

Classified#:	645
Date Posted:	9/16/2010
Make:	Becton-Dickinson
Model:	FACStar Plus
Age:	13 to 15 years
Accessories:	Refer to description and pictures
History:	Pre-owned by Hospital Research Lab
Dimensions:	n/a
Weight:	900 lbs
Location:	Canada
Price:	Inquire
Payment Method:	Wire Transfer
Warranty:	As Is Working
Hits:	385

RELATED PROCEEDING APPENDIX

The appellants have not filed any other related appeals and there are no BPAI or court decisions related to the instant application.